Review Article

Blood Management Strategies for Total Knee Arthroplasty

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Abstract

Perioperative blood loss during total knee arthroplasty can be significant, with magnitudes typically ranging from 300 mL to 1 L, with occasional reports of up to 2 L. The resultant anemia can lead to severe complications, such as higher rates of postoperative infection, slower physical recovery, increased length of hospital stay, and increased morbidity and mortality. Although blood transfusions are now screened to a greater extent than in the past, they still carry the inherent risks of clerical error, infection, and immunologic reactions, all of which drive the need to develop alternative blood management strategies. Thorough patient evaluation is essential to individualize care through dedicated blood management and conservation pathways in order to maximize efficacy and avoid associated complications. Interventions may be implemented preoperatively, intraoperatively, and postoperatively.

JAAOS Plus Webinar

Join Dr. Levine, Jay Lieberman, MD, and John Callaghan, MD, for the *JAAOS* interactive webinar discussing "Blood Management Strategies for Total Knee Arthroplasty," on Wednesday, July 23, at 9 PM Eastern.

To join and to submit questions in advance, please visit the OrthoPortal website: http://orthoportal.aaos.org/jaaos/

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Total knee arthroplasty (TKA) is among the most commonly performed elective procedures in the United States. The prevalence of TKA has increased dramatically due to both an aging population and a rise in per capita utilization. Perioperative blood loss and allogenic transfusions associated with TKA can potentially result in substantial cost increases and significant complications, such as postoperative infection, delayed physical recovery, longer hospital stays, and increased mortality.[1] These complications may be magnified in patients with preexisting medical comorbidities, including cardiac, pulmonary, and renal disease. Perioperative blood loss associated with primary TKA procedures has been reported to range from approximately 300 mL to 1 L.[2,3] When hidden losses are considered and when calculated blood loss is based on hemoglobin change, magnitudes of 1 to 2 L[4,5] can be translated into transfusion rates ranging as high as 63%[6] to 94%.[3]

Historically, allogenic transfusion has been the standard method of managing acute blood loss anemia secondary to TKA. Despite stringent testing parameters, allogenic transfusion carries significant inherent risks, including clerical error, infection due to the rare complication of inoculated allogenic blood as well as the immunologic modulation caused by allogenic transfusion,[7] contamination, and immunologic reactions[8] (Table 1). Due to potential complications and adverse events associated with blood loss and allogenic transfusion, it is imperative to explore blood conservation and management strategies to reduce perioperative bleeding and to find alternative replacement options.

Despite a plethora of perioperative blood management strategies, little peer-reviewed literature is available to support the use of such modalities. Additionally, they may add significant expense to the overall procedure, which may limit widespread acceptance, given the current emphasis on

Table 1

Risks of Allogenic Blood Transfusion by Complication Type[8]

Complication	Incidence
Infectious	
HIV infection	1:1,900,000
HBV infection	1:180,000
HCV infection	1:1,600,000
Bacterial contamination	1:3,000
Cardiopulmonary	
TACO	1:5,000
Acute lung injury	1:50,000
Systemic	
Fever or allergic reaction	1:200
Hemolytic transfusion reaction	1:6,000
Fatal hemolytic reaction	1:1,000,000
Anaphylaxis	1:50,000

HBV = hepatitis B virus, HCV = hepatitis C virus, TACO = transfusion-associated circulatory overload

Table 2

Perioperative Blood Management Strategies

Preoperative
Vitamin supplementation
Epoetin α
Preoperative autologous donation
Intraoperative
Tourniquet
Bipolar sealant
Argon-beam coagulation
Topical hemostatic agents
Antifibrinolytics
Hemodilution
Postoperative
Reinfusion systems
Transfusion protocols

cost reduction and containment in primary TKA (Table 2). We present a comprehensive review of currently available technologies, medications, and devices available to surgeons performing TKA. An effort was made to include the highest quality peer-reviewed studies. In the absence of level I and II evidence, level III and IV studies were assessed.

Preoperative Assessment and Planning

To ensure prudent perioperative blood management, it is crucial to start with a thorough preoperative assessment to determine the patient's physiologic status, nutritional condition, starting blood levels, body weight, and cardiovascular disease status.[9] A detailed medical evaluation should take place no less than 3 weeks before surgery to allow adequate time for proper intervention and planning.[9] Based on the anticipated blood loss of surgery, preoperative hemoglobin levels, medical evaluation, nutritional status, patient comorbidities, and the expected response to an acute anemic state, the surgeon can develop an individualized blood management protocol or follow published algorithms.[9-11] Patients with preoperative anemia should be evaluated to determine the underlying etiology, and consideration should be given to evaluation by a hematologist and/or the appropriate subspecialist before proceeding with TKA. In a recently published retrospective study of 2,281 patients who underwent TKA, Ahmed et al[12] found through a regression analysis that patient age ($P < 0.001$), preoperative hemoglobin ($P < 0.001$), body weight ($P = 0.009$), and lateral retinacular release ($P < 0.001$) were all significant independent factors for predicting the need for blood transfusion.

Preoperative Strategies

Preoperative blood management strategies are aimed at optimizing hemoglobin levels so that patients can better tolerate the physiologic stress associated with surgical blood loss. In addition, these strategies may augment the postoperative erythropoietic response to blood loss and hasten the recovery process. Preoperative strategies include iron, folate, and vitamin B_{12} supplementation, erythropoietin (EPO), and preoperative autologous donation (PAD).

Vitamin Supplementation

Iron, folate, and vitamin B_{12} are major building blocks involved in the generation of red blood cells (RBCs). Deficiencies in these compounds have been associated with corresponding anemia. A preoperative medical workup for anemia should be completed before proceeding with an elective TKA.

In a series of patients undergoing TKA, preoperative supplementation with iron (256 mg/day), vitamin C (1,000 mg/day), and folate (5 mg/day) 30 to 45 days before surgery resulted in a lower transfusion rate than did no such supplementation (5.8% and 32%, respectively).[13] However, in a prospective cohort study of 87 patients, preoperative iron supplementation at a dosage of 300 mg three times daily for ≥3 weeks was not effective in preventing reduced hemoglobin or hematocrit after hip or knee arthroplasty.[14] Further, iron supplementation was associated with a high level of

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side effects, including constipation (33.3%), heartburn (13.8%), and abdominal pain (12.6%).

Although the current evidence for it is not strong, limited data seem to favor maximizing preoperative levels of anemia-associated vitamins. In the absence of a specific deficiency, however, the routine use of iron supplementation is not recommended.

Table 3

Epoetin α Recommended Dosing[15]

Dosing	Schedule
600 IU/kg	4 doses: Preoperative days 21, 14, 7, 0
300 IU/kg	15 doses: Daily—preoperative day 10 to postoperative day 4
150 IU/kg[a]	9 doses: Daily—preoperative day 5 to postoperative day 3

[a] Alternative dosing for augmentation of postoperative response to acute blood loss

Erythropoietin

EPO is a natural glycoprotein that is produced by renal pericapillary cells in response to decreased oxygen tension, which occurs in physiologic states such as anemia or chronic obstructive pulmonary disease. EPO acts on bone marrow to increase the rate of RBC differentiation and maturation, thereby increasing total RBC mass. EPO is available in its recombinant form, epoetin α, which has been widely used in patients with chronic anemia associated with chemotherapy or renal disease. Several dosing regimens have been suggested in the literature, including both preoperative and postoperative protocols[15] (Table 3). In the setting of arthroplasty, EPO has been used in three perioperative scenarios: alone, in conjunction with PAD, and postoperatively.[16] The selective use of preoperative EPO has been shown to be effective when large amounts of blood loss are anticipated.[17]

In multiple studies, EPO has demonstrated significant benefit as a preoperative blood management technique with superior efficacy compared with placebo, PAD, and reinfusion systems (Table 4). Despite these findings, EPO has been used effectively in the setting of TKA in combination with PAD.[16] The primary disadvantage to the routine use of EPO is cost. The average price per patient is equivalent to two to three units of PAD or three to four units of allogenic blood. Nevertheless, the use of EPO is recommended in patients at higher risk of allogenic transfusion, such as those with low preoperative hemoglobin levels (<13 g/dL) or low body weight (<50 kg) and in surgeries in which considerable blood loss is expected. Thus, the authors lend strong consideration for its use in patients who are undergoing revision surgery in the setting of preoperative anemia, in those undergoing bilateral surgery, and in those who begin with a hemoglobin level of <13 g/dL.

Preoperative Autologous Donation of Blood

PAD involves the preoperative procurement of one to two units of the patient's blood before surgery. The autologous units are then used as a substitute for allogenic units either intraoperatively or postoperatively. Preoperative donation should occur at least 3 weeks before surgery to allow time for an appropriate recovery of hemoglobin levels. Published evidence is mixed regarding the efficacy, cost effectiveness, and recommendations of PAD. Consequently, the routine use of PAD has fallen out of favor, and it is no longer considered a staple in the armamentarium for addressing perioperative blood management in unilateral TKA.

The literature lacks consensus regarding the utility of PAD. Deutsch et al[18] compared PAD with preoperative EPO in a randomized controlled trial (RCT) of 50 patients with a preoperative hemoglobin level between 10 and 13 g/dL. The transfusion rate was 8% in the PAD group and 28% in the EPO group. However, the EPO dosing used in this study has been questioned and may not have been sufficient. Alternatively, Keating and Ritter[11] demonstrated that the allogenic transfusion rate was lower with EPO (with a more commonly used dosing regimen) than with PAD.

PAD has been scrutinized because its use results in iatrogenic reduction in preoperative hemoglobin stores and requires advanced planning, storage, and preparation of the donated units.[11,18,21] Thus, there is a danger of clerical error, bacterial contamination, and infection.[9,22] Inappropriate use of PAD also results in several unused units of blood, with reports describing a >50% incidence.[9,22] Additionally, PAD is associated with an increased risk of postoperative transfusions (allogenic or autologous),[9] coagulopathy, fluid overload, and discarded units.[22] PAD may have the greatest benefit in patients with normal preoperative hemoglobin levels (>14 g/dL) who are scheduled to undergo surgery with a large amount of expected blood loss, such as revision surgery or bilateral TKA.[10] However, PAD may be performed in any patient with a hemoglobin level >11 g/dL and weighing >50 kg (>110 lb) if performed with sufficient time before surgery.[22] In a survey performed at the 2009 Annual Meeting of the American Association of Hip and Knee Surgeons, 85% of attendees reported that they "virtually never" collect autologous blood preoperatively.[23]

Table 4

Level II Randomized Controlled Trials on the Use of Epoetin α as a Blood Management Strategy in Arthroplasty

Study	No. of Patients	Comparison	Allogenic Transfusion Rate	Significance
Weber et al[19]	695	EPO vs routine care	EPO, 12%; routine care, 46%	$P < 0.001$
Stowell et al[20]	490	EPO vs PAD	EPO, 12.9%; PAD, 19.2%	$P = 0.078$
Deutsch et al[18]	50	EPO vs PAD	EPO, 28%; PAD, 8%	$P = 0.138$
Bezwada et al[16]	240	EPO preoperatively + PAD vs EPO preoperatively vs EPO postoperatively	EPO preoperatively, 11%; EPO preoperatively + PAD, 28%; EPO postoperatively, 33%	$P < 0.05$

EPO = epoetin α, PAD = preoperative autologous donation

Table 5

Comparison of Level II Randomized Controlled Trials on Acute Normovolemic Hemodilution

Study	No. of Patients	Comparison	Measure	Outcome	Significance
Olsfanger et al[25]	30	ANH vs control	Transfused units	ANH: 2 hr (7 units), 6 hr (5 units); control: 21	$P < 0.024$
Goodnough et al[24]	32	ANH vs PAD	Collected units	ANH, 2.2; PAD, 1.4	$P = 0.003$
			Percentage of reinfused units	ANH, 94%; PAD, 61%	$P = 0.13$
			Allogenic rate (primary TKA)	ANH, 25%; PAD, 8%	$P = 0.53$
Juelsgaard et al[26]	28	ANH vs control	Blood loss (transfusion rate)	ANH, 1,306 mL (50%); control, 1,026 mL (58%)	NS

ANH = acute normovolemic hemodilution, NS = not statistically significant, PAD = preoperative autologous donation, TKA = total knee arthroplasty

Although PAD is an attractive option for the management of postoperative anemia, the associated risks and cost may outweigh the potential benefits. The literature does not appear to support the routine use of PAD in the setting of primary TKA. However, level II research suggests that it may play a role in the setting of revision or bilateral TKA.[24]

Intraoperative Strategies

Intraoperative strategies focus on reducing the amount of blood loss during and immediately after surgery. Options include the use of a tourniquet, electrocautery, antifibrinolytics, topical hemostatic agents, acute normovolemic hemodilution (ANH), and cell salvage and reinfusion systems. Although intraoperative strategies to reduce blood loss are appropriate for all patients, the cost of such modalities must be weighed against their documented efficacy in the peer-reviewed literature.

Hemodilution

ANH is similar to PAD; however, with ANH, blood is harvested just before or at the time of surgery. The removed volume of blood is then replaced with colloid, which results in a lower concentration of RBCs in the blood that is subsequently lost. The donated blood may then be reinfused perioperatively. The advantages of ANH over PAD include the need for less planning as well as reduced risk of clerical error, bacterial contamination, and wasted units.[9] The disadvantages of ANH are increased time in the operating room, higher cost, and the potential for greater blood loss.[25]

Table 5 describes the available literature regarding the use of ANH in total joint arthroplasty. Because the literature on the use of ANH is conflicting and because the process is relatively cumbersome, the routine use of ANH has largely been abandoned except in extreme cases (ie, patients who refuse allogenic blood products based on religious beliefs or practice).

Tourniquet

Tourniquets are routinely used in TKA. At our institution, we often inflate tourniquets to 100 to 150 mm Hg greater than the patient's systolic blood pressure. Although the impact of tourniquet use is somewhat controversial, some surgeons believe that it allows for a bloodless surgical field, improved cement interdigitation, and decreased surgical time.[27]

In an RCT of 20 patients treated with bilateral TKA, Thorey et al[28] released the tourniquet before wound closure on one knee and delayed release until after wound closure on the other. A significant reduction in surgical time was noted with delayed tourniquet release compared with tourniquet release prior to wound closure (51 and 58 minutes, respectively). No difference between the groups was found with regard to perioperative blood loss or complications at 6-month follow-up. A second RCT of 46 TKAs (43 patients) confirmed that timing of tourniquet release had no effect on blood loss, change in hemoglobin level, or transfusion requirements.[29]

A meta-analysis published in 2011 supports the finding that use of a tourniquet results in shorter surgical time; however, it also revealed that thromboembolic events occurred at a higher rate with tourniquet use than without (13% and 6.1%, respectively).[30] In another meta-analysis, delayed tourniquet release was related to a higher rate of postoperative wound complications requiring reoperation compared with early release (3.1% and 0.3%, respectively).[31] The higher rate of complications is believed to be due to an increased rate of lateral retinacular release, which occurs at a 1.5 to 9 times higher rate when patellar tracking is assessed with the tourniquet inflated. Lateral release may result in greater hematoma formation due to disruption of the blood supply from the lateral geniculate arteries.[31]

Tourniquet use also has the potential to cause local muscle damage, neurapraxia, and systemic release of thrombolytic factors upon deflation. Although in general these complications are self-limited, tourniquet use should be avoided in patients with significant peripheral vascular disease.

A poll conducted at the 2009 Annual Meeting of the American Association of Hip and Knee Surgeons regarding common practices of orthopaedic surgeons showed that 95% use a tourniquet throughout the entire case, of whom 37% use one routinely, regardless of concomitant peripheral vascular disease.[23] In a review of the Mayo Clinic total joint registry, a significant risk for thrombosis of an ipsilateral arterial bypass graft was noted regardless whether a tourniquet was used during TKA.[32] Patients with risk factors for arterial complications, such as history of arterial insufficiency, absence of pedal pulses, suspected popliteal aneurysm, and radiographic evidence of calcification, should be referred to a vascular surgeon for preoperative recommendations. Although tourniquet use is controversial, we concur with the recent literature supporting its use during primary TKA.

Electrocautery: Bipolar Sealants

Unlike standard monopolar electrocautery, bipolar sealants require the use of bipolar radiofrequency. The proposed advantage of bipolar devices is the coupling of the continuous flow of saline with electrocautery. The tip remains relatively cool, which allows collagen shrinkage in blood vessels and a reduction in associated tissue damage. In TKA, bipolar sealants are used on the capsule, meniscal attachment sites, and synovium to achieve preemptive hemostasis. Data on this modality are limited. This modality has the potential to substantially increase surgical costs.

A few well-designed studies have refuted the efficacy of bipolar cautery in primary TKA, describing no differences in transfusion requirements, blood loss, change in hemoglobin level, length of hospital stay, narcotic use, wound drainage, pain scores, or functional outcomes[2,33] (Table 6). The higher cost of bipolar cautery and the lack of significant peer-reviewed literature have led us to question the routine use of this modality in primary TKA.

Argon-beam Coagulation

Argon-beam coagulation (ABC) uses ionized argon gas to deliver radiofrequency cautery to the tissue. Argon gas blows blood away to improve visibility and decrease the diameter and depth of eschar formation, resulting in less charring and tissue damage. ABC has been shown to be an effective means of achieving hemostasis in a variety of surgical specialties. However, there is no orthopaedic literature regarding its use in arthroplasty. Due to the relatively low cost (approximately $4 per disposable pencil), ABC warrants further investigation for use in orthopaedic procedures.

Antifibrinolytic Agents

Antifibrinolytic agents act to decrease the effects of plasmin, thereby decreasing the rate of fibrinolysis and stabilizing fibrin clots to result in more stable hemostasis (Figure 1). Such agents include ϵ-aminocaproic acid, aprotinin, and tranexamic acid (TA). Aprotinin is a serine protease inhibitor (eg, plasmin), and ϵ-aminocaproic acid is a lysine derivative that prevents plasmin activation and fibrin binding. Peer-reviewed literature is scarce regarding the use of ϵ-aminocaproic acid and aprotinin in TKA, and consensus recommendations cannot be offered at this time. However, abundant evidence exists regarding the efficacy of TA in TKA.

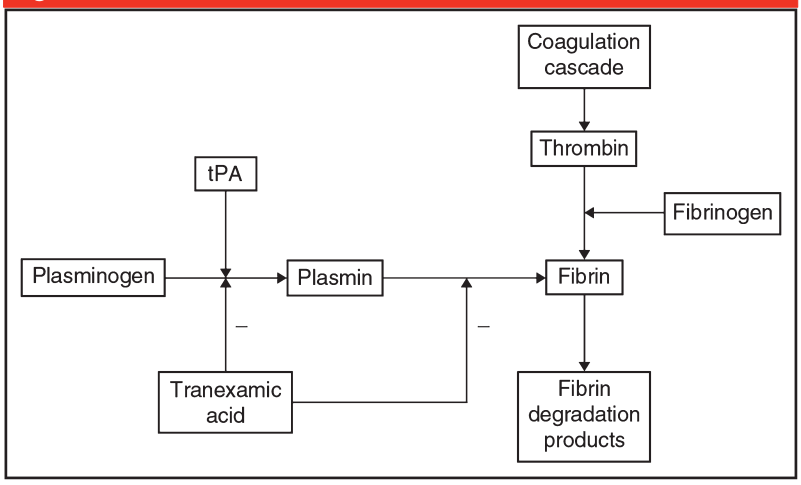
Table 6

Comparison of Bipolar and Monopolar Electrocautery in Randomized Controlled Trials

Study	Level of Evidence	Number	Measure	Outcome	Significance
Marulanda et al[5]	I	69 TKAs (B, 35; M, 34)	Blood loss	B, 1,254 mL; M, 1,553 mL	$P = 0.03$
			Hemoglobin decrease	B, 2.9 g/dL; M, 3.5 g/dL	$P = 0.04$
			Transfusion rate	B, 29%; M, 47%	$P = 0.0186$
Barsoum et al[2]	I	140 patients (THA)	Blood loss	B, 315.2 mL; M, 368.5 mL	$P = 0.2$
			Hemoglobin change	B, 5.4 g/dL; M, 5.3 g/dL	$P = 0.1$
			Transfusion rate	B, 21.1%; M, 20.3%	$P = 0.9$
Plymale et al[33]	II	113 patients	Hemoglobin change	B, 3.5 g/dL; M, 3.5 g/dL	$P = 0.78$
			Transfusion rate	B, 40%; M, 36%	$P = 0.67$
			Drain output	B, 776 mL; M, 778 mL	$P = 0.97$

B = bipolar electrocautery, M = monopolar electrocautery, THA = total hip arthroplasty, TKA = total knee arthroplasty

Figure 1



Algorithm of the tranexamic acid mechanism of action. The minus signs signify the inhibitory effects of tranexamic acid on plasminogen and plasmin. tPA = tissue-type plasminogen activator

TA is a lysine derivative that competitively blocks plasmin-binding sites on fibrin, thereby decreasing fibrinolysis (Figure 1). TA is available in oral, intravenous, intramuscular, and intra-articular formulations. In a recently published RCT of 150 patients treated with TKA, the use of TA was shown to result in significantly reduced mean blood loss, change in hemoglobin level, and transfusion rates.[3] These results were corroborated by a recent meta-analysis that evaluated 15 RCTs in which TA was used in the setting of TKA.[34] The authors of the study reported significantly less blood loss and fewer blood transfusions in the patients treated with TA compared with patients treated with placebo. Notably, no difference was found in deep vein thrombosis (DVT) or pulmonary embolism between the two groups. Various dosing regimens exist, and there is no consensus on the best protocol; however, multiple dose regimens and weighted dosing appear to be the most effective.[35,36] Recent studies have verified that TA is safe with all DVT prophylaxis regimens, does not increase perioperative complications, does not alter prothrombin time or activated partial thromboplastin time, and is not associated with increased rates of DVT or pulmonary embolism.[34,36]

Based on these findings, on reports of reductions in the cost of blood conservation therapy, and on overall agreement in efficacy, the routine use of TA in TKA is recommended, particularly in patients at increased risk of transfusion, in patients with preoperative hemoglobin levels <13 g/dL, and in cases with an expected large amount of blood loss (eg, bilateral surgery). Contraindications to TA include history of stroke, venous thromboembolism, allergy, and severe coronary artery disease. A specific dosing regimen cannot be recommended given the varying literature and the heterogeneity of current data. At our institution, we routinely use 1,000 mg of TA in

patients who do not meet the aforementioned contraindication criteria. We administer single-dose TA intravenously, typically just before component placement or tourniquet release.

Topical Hemostatic Agents

Topical hemostatic agents include collagen agents, plant-derived cellulose, fibrin sealants, platelet-rich plasma (PRP), and platelet-poor plasma. Collagen agents stimulate the intrinsic coagulation pathway to encourage hemostasis. Fibrin sealants typically have two separate mixtures of human coagulation proteins. The mixture that contains fibrinogen and factor XIII is combined with the second mixture, which contains thrombin and calcium, to create a fibrin seal. PRP is generated by centrifuging the patient's blood to isolate the components of plasma rich in platelets, growth factors, and vasoactive substances. It has been proposed that PRP improves hemostasis, wound healing, and recovery. The platelet-poor plasma isolate from the centrifuge may be combined with thrombin and calcium to create an autologous fibrin sealant.

In an RCT of 90 patients who underwent TKA, Notarnicola et al[6] compared the effects of varying dosing of fibrin sealants (ie, 10 mL, 5 mL, none). They reported encouraging results, with no significant difference between the two fibrin sealant study groups. Others have debated the successful results of autologous platelet gels and commercially available fibrin sealants and have questioned the utility of this modality for routine use in TKA.[37] Similarly, in an RCT in which the use of the thrombin-based sealant Floseal (Baxter International) during primary TKA was evaluated, 196 patients were randomized to receive the topical spray intraoperatively (97 treated patients, 99 control subjects).[38] No clinically significant differences were exhibited between postoperative drain outputs, hemoglobin changes, transfusion rates, or postoperative complications.

Although well-designed published studies clearly demonstrate some level of efficacy with topical hemostatic agents (eg, potential reductions in hemoglobin change, early range of motion, length of stay), further study is needed to determine whether topical hemostatic agents are cost effective. Currently, these agents are relatively expensive. Floseal costs approximately $160 per 5-mL syringe, and fibrin sealants cost approximately $100 to $150 per mL of fibrinogen[39] (Table 7).

Based on the conflicting results of the level I, II, and III studies, the routine use of topical hemostatic agents in TKA does not seem prudent. Further research on topical hemostatic treatments is necessary before their use can be encouraged.

Table 7

Average Cost of Various Blood Management Modalities

Modality	Average Cost (US)
Erythropoietin	$1,200–2,000/patient
Aprotinin	>$1,000/dose
Red blood cell salvage	$800/case
Autologous blood donation	$700/unit of blood
Allogenic transfusion	$500/unit of blood
Reinfusion drains	$500/drain
Fibrin sealants	>$450/case
Radiofrequency tissue sealer	$400/case
Argon-beam coagulation	$100/case
Tranexamic acid	≈$80/dose

Data taken as an average of three hospitals (one urban academic center and two suburban private hospitals).

Postoperative Strategies

Postoperative strategies, such as the use of reinfusion systems and guided transfusion protocols, serve as alternatives to allogenic transfusion.

Reinfusion Systems

Reinfusion systems may be used intraoperatively or postoperatively to collect shed blood. The shed blood is then filtered, washed, and reinfused within 6 to 8 hours after collection. Such systems have the proposed advantages of reducing postoperative hematomas, minimizing wound complications, and producing washed blood that serves as an alternative to allogenic blood. Although reinfusion systems are an inherently attractive alternative to allogenic transfusion, the purported benefits must be weighed against the potential complications, which include coagulopathy, contamination, and expense. The etiology of this coagulopathy is tied to the altered composition of the reinfused blood, with reported elevations in fibrin split products and inflammatory cytokines, such as tumor necrosis factor-α and interleukins.[40,41]

In an RCT of 77 patients who underwent TKA, Moonen et al[40] compared the use of a regular drain with use of a postoperative reinfusion system and found a notable decrease in allogenic transfusion requirements with the reinfusion system (1 of 45 and 5 of 32 patients, respectively). However, in an RCT of 100 patients who underwent TKA, Martin and von Strempel[41] found that the use of a reinfusion system did not result in lower transfusion requirements. Additionally, the use of a closed suction drain system correlated with significantly higher postoperative blood loss (1,424 and 247 mL, respectively).

The increase in blood loss was explained by Matsuda et al.[42] Their study on shed blood collection systems found that unwashed shed blood had increased levels of tissue-type plasminogen activator and lower levels of fibrin compared with

Table 8

Level II Studies on Postoperative Reinfusion Drain Systems

Study	No. of Patients	Comparison	Measure	Outcome	Significance
Moonen et al[40]	160 (TKA and THA)	Reinfusion drain vs control	Allogenic transfusion rate	Reinfusion, 6%; control, 19%	$P = 0.0015$
			Febrile reaction rate	Reinfusion, 18%; control, 20%	
Martin and von Strempel[41]	100	Reinfusion vs control	Blood loss	Reinfusion, 1,424 mL; control, 247 mL	$P < 0.001$
			Allogenic transfusion rate	Reinfusion, 50%; control, 36%	$P > 0.05$
			Mean ROM 3 mo postoperative	Reinfusion, 99°; control, 103°	NS
			Mean Insall score 3 mo postoperative	Reinfusion, 155; control, 159	NS
			Complications	Reinfusion, 28%; control, 30%	NS
Al-Zahid and Davies[43]	102	Reinfusion vs closed suction vs no drain	Hemoglobin change	Reinfusion, 2.53 g/dL; closed suction, 2.72 g/dL; no drain, 2.84 g/dL	$P = 0.41$
			Allogenic transfusion rate	Reinfusion, 8%; closed suction, 10%; no drain, 6%	NS

NS = not statistically significant, ROM = range of motion, THA = total hip arthroplasty, TKA = total knee arthroplasty

normal blood. A positive correlation was found between the tissue-type plasminogen activator level of shed blood and the volume of postoperative drainage, which led the authors to conclude that reinfusion of unwashed shed blood had a fibrinolytic effect and led to increased postoperative drainage.

In a prospective RCT, Al-Zahid and Davies[43] compared closed suction drains, reinfusion drains, and no drain. They found no differences in change in hemoglobin level, transfusion rates, or American Knee Society score functional improvement.

The literature shows mixed efficacy regarding the ability of reinfusion systems to reduce allogenic transfusions, with a greater number of studies reporting no significant effect.[40,41] There is also evidence that reinfused shed blood may increase fibrinolytic activity and total wound drainage.[7,42] Although reinfusion systems are used frequently at our facility, recent conflicting data suggest that their routine use may not be warranted (Table 8).

Transfusion Triggers

One of the most effective means to reduce the rate of allogenic blood transfusion is to initiate stringent transfusion protocols. Historically, it was common to transfuse based on the "10/30 rule," in which patients were automatically transfused if their hemoglobin level fell below 10 g/dL or their hematocrit level fell below 30%. The current literature indicates that much lower transfusion triggers are acceptable without adverse consequences.

In a review comparing a restrictive transfusion algorithm with a more liberal policy in 603 patients who underwent elective TKA or total hip arthroplasty, So-Osman et al[44] reported that the allogenic transfusion rate decreased with the former guidelines, from 0.86 unit per patient to 0.78 unit per patient, with no changes in hospital stay, cardiovascular morbidity, or mortality. In comparison with the standard transfusion policy, they found a decrease of 30% and 41% at two hospitals, respectively, and an increase of 39% at a third hospital, using their more restrictive algorithm. In the restrictive algorithm, low-risk patients were younger than 50 years, with a hemoglobin transfusion trigger of 6.4 g/dL, whereas patients in the intermediate- and high-risk groups differed from each other in terms of age, hemoglobin level, and time from surgery.

Available controlled trials on TA and transfusion triggers indicate that there is no benefit in administering a blood transfusion for persons with

hemoglobin levels >8 g/dL, regardless of cardiovascular risk.[45,46] The American Association of Blood Banks clinical practice guideline on transfusion recommends the use of restrictive protocols in which transfusion is considered only in patients whose hemoglobin level is ≤8 g/dL.[47] The guideline also recommends the use of symptoms as well as hemoglobin level in determining when to use transfusion. The restriction of transfusion to patients with hemoglobin levels <8 g/dL is supported by Carson et al,[48] who reviewed 8,787 patients with hip fracture. They found transfusion to have no effect on mortality in patients with hemoglobin levels as low as 8 g/dL. In a small study of healthy patients, Weiskopf et al[49] demonstrated that hemoglobin levels as low as 5 g/dL could be tolerated without consequence, provided the volume was replaced with crystalloid.

The importance of taking into account patients' symptoms when determining whether to transfuse was exemplified by Robinson et al.[50] In their 6-year observational study of 1,169 patients who underwent total hip arthroplasty, transfusion was performed only in cases of symptomatic anemia. This practice of transfusion based on symptoms resulted in reduced average hemoglobin level at the time of transfusion, from 7.9 to 7.3 g/dL, and a 55% reduction in blood utilization. There was no change in complication rates.

The evidence for lower transfusion triggers and use of symptoms in algorithms when determining when to transfuse is summarized in current guidelines. Per current guidelines, it is recommended that patients with hemoglobin levels <6 g/dL receive RBC transfusion and that patients with hemoglobin levels >10 g/dL not receive a transfusion, regardless of physiologic status.[47] For patients with hemoglobin levels of 6 to 10 g/dL, transfusion should be based on expectation of continued blood loss, intravascular volume status, cardiovascular reserve, and response to anemia. In these patients, vital signs and electrocardiogram must be monitored for evidence of inadequate oxygenation, and volume should be replaced with crystalloid. Even with the evidence and guidelines that advocate the incorporation of patient factors and symptoms when determining transfusion algorithms, one review of guidelines and studies on transfusion practices indicated that 85% of transfusions following primary hip and knee replacement could be predicted by hemoglobin nadir alone and that other factors, such as coronary artery disease, had little impact.[51]

Based on the available literature, we recommend that transfusion be avoided in any patient with a hemoglobin level >8 g/dL and that transfusion be used in all patients with hemoglobin levels <6 g/dL. For persons with hemoglobin levels between 6 and 8 g/dL, the decision to transfuse should be based on ongoing losses, patient factors, cardiovascular risk, and symptoms due to anemia. Orthopaedic surgeons should consider consulting their hospitalist and internal medicine colleagues, as needed.

Summary

A variety of blood management and conservation strategies are available, with limited high-level evidence to support their routine use. These strategies should be combined and tailored specifically to each patient based on the preoperative evaluation, surgical blood loss, and response to anemia. Preoperatively, administration of EPO can be efficacious either in conjunction with PAD or in anemic patients. Intraoperatively, tourniquet use and TA receive higher consideration at our institution than do cautery and topical options. Postoperatively, it is imperative to closely monitor the patient's response to anemia and use appropriate transfusion triggers to avoid unnecessary blood transfusions.

The routine use of PAD, bipolar sealants, and reinfusion systems is not supported by the current literature. Further high-quality RCTs are necessary to determine what regimens will ultimately be used in isolation or as combination therapy to minimize the number of, as well as the potential, complications and side effects associated with transfusion and bleeding. Although minimizing transfusion rates is an important facet of modern TKA, it is important to weigh the costs and benefits before routinely implementing a specific blood management and conservation strategy.

References

Evidence-based Medicine: Levels of evidence are described in the table of contents. In this article, references 1, 2, 4-6, 30, 34, 36, and 38 are level I studies. References 3, 8, 11, 13, 16, 18-20, 22, 24-26, 28, 29, 31, 33, 35, 37, 40-44, 47, and 49 are level II studies. References 10, 12, 14, 21, 32, 48, and 50 are level III studies. References 9 and 27 are level IV studies. References 7, 23, and 39 are level V expert opinion.

References printed in **bold type** are those published within the past 5 years.

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